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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/727,619	PAHL, HEIKE	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4 and 9-29* is/are pending in the application.

4a) Of the above claim(s) *9-12, 14, 16-17, 19-20, 23, 25-26, 28-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,13,15,18,21,22,24 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,4 and 9-29* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/830,189.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/5/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, drawn to an isolated polypeptide of SEQ ID NO: 2, an isolated polynucleotide of SEQ ID NO: 1, process for detecting polycythaemia vera in the reply filed on 15 May 2006 is acknowledged. The traversal is on the ground(s) that a search of all the claims would comprise overlapping subject matter, and it would not be an undue burden on the examiner to carry out a search. Applicant also argues that Group II should be examined with elected Group I inasmuch the method of claim 13, drawn to the same, has been restricted under Group I. Applicant contends that the patentability of the method of use of Group V is based at least on the patentability of the claimed polypeptide, and mandates maintaining these claims with Group I. This is not found persuasive because, as discussed in the previous Office Action (18 April 2006), the products of Group I can be used in materially different methods other than the methods of Groups II, IV-V, such as to generate antibodies, cell culture assays, or diagnostic assays. Additionally, Groups I-II, IV-V are different methods requiring different products and method steps, wherein each is not required, one for another. As discussed at pg 3-4 of the previous Office Action, and reiterated herein, Group I requires search and consideration of detecting the PRV-1 polynucleotide using RT-PCT or blotting, which is not required by the other inventions. Group II requires search and consideration of utilizing antibodies and the polypeptide in an immunoassay to detect polycythaemia vera, which is not required by the other inventions. Group V requires search and consideration of using the polypeptide of SEQ ID NO: 2 as a growth factor to treat/multiply cells ex vivo or in vitro, which is not required by the other inventions. Thus, each method is divergent in materials and steps.

Furthermore, the distinct steps and products require separate, distinct, and non-coextensive searches. As such, it would be burdensome to search the inventions of Groups I-V together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-12, 14, 16-17, 19-20, 23, 25-26, and 28-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 15 May 2006.

Claims 1, 4, 13, 15, 18, 21, 22, 24, and 27 are under consideration in the instant application.

Priority

1. It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/830,189, filed 8/06/2001. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the

pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Drawings

2. Figures 1-2 are objected to because tables and sequence listings that are included in the specification are, except for applications filed under 35 U.S.C. 371, not permitted to be included in the drawings (see 37 CFR 1.83(a) and 1.58(a); MPEP § 608.02). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

3. The disclosure is objected to because of the following informalities:

3a. As provided in 37 CFR 1.77(b) and MPEP § 601(I), the specification of a utility application should include different sections. Each of section should appear in upper case, without underlining or bold type, as a section heading. In the instant case, there are no sections

indicating, *for example*: "BACKGROUND OF THE INVENTION", "BRIEF SUMMARY OF THE INVENTION", "DETAILED DESCRIPTION OF THE INVENTION", "EXAMPLES".

Appropriate correction is required.

Claim Objections

4. Claims 13 and 18 are objected to because of the following informalities:

4a. Line 1 of claim 18 is missing the term "a" before "polypeptide".

4b. Regarding claim 13, the acronym "PRV-1" should be spelled out for clarity.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 and 35 USC § 101

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 18 provides for the use of polypeptide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

7. Claim 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e.,

results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 24 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to kits for detecting haematopoietic disturbances such as polycythaemia vera comprising a PRV-1 polypeptide (cl. 24, 27). The specification discloses the PRV-1 polypeptide of SEQ ID NO: 2, which is structurally related to surface receptors of the uPAR/Ly6 family. Based on this structural similarity, the specification asserts that PRV-1 can transduce mitogenic signals, and that overexpression of PRV-1 on granulocytes contributes to hyperproliferation of granulocytes (p. 5, lines 26-32). However, the specification contains no working examples to substantiate this assertion, and the art does not support this conclusion. See Pahl (2000, Eur. J. Biochem. 267:3395-3401) wherein it is stated that:

> "PRV-1 shows structural similarity to the uPAR/Ly6/CD59/snake toxin-receptor superfamily. These molecules fulfill a **diverse** set of functions, for example during leukocyte activation, prevention of erythroid autologous lysis and in bone morphogenesis. **Therefore, PRV-1 function cannot be inferred from its membership in this receptor family**." (p. 3399, emphasis added, citations omitted).

Furthermore, the specification asserts that the PRV-1 polypeptide can be used diagnostically, wherein an overproduction of PRV-1 protein is correlated with a diagnosis of polycythaemia vera (p. 7). However, this diagnostic use is not enabled by the specification. There are no working examples of this diagnostic use. Importantly, the literature clearly shows that, whereas PRV-1 **mRNA** is overexpressed in polycythaemia vera patients, there is no significant difference in PRV-1 **polypeptide** expression levels between polycythaemia vera patients and healthy control subjects. See Klippel et al., 2002, Blood 100 :2441-2448 ; especially Abstract at p. 2441 and "PRV-1 protein expression is not consistently altered in patients with polycythaemia vera" (pp. 2445-2446). Thus the art is directly contradictory to this asserted use.

Due to the large quantity of experimentation necessary to determine how to use PRV-1 polypeptide to diagnose any haematopoietic disturbance, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the contradictory state of the prior art (see Pahl and Klippel et al.), the unpredictability of which disease might be associates with changes in PRV-1 levels or forms, and the breadth of the claims which fail to recite limitations regarding how a specific change in PRV-1 levels or forms correlates with any specific disease, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

9. Claims 1, 15, 18, 24, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed inventions wherein the recited polypeptide comprises SEQ ID NO: 2 and the recited activity for the drug is to promote the formation of erythroid cells, does not reasonably provide enablement for drugs comprising

fragments of SEQ ID NO: 2, or drugs that have effects on any pancytopenia or pancytopathy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims recite specific amino acid sequences of SEQ ID NO: 2, including fragments containing at least 50 amino acids, drugs comprising the same, and use of the polypeptide of claim 1 for producing a drug having effects on any pancytopenia or pancytopathy. The specification defines pancytopenias and pancytopathies at pg 11, lines 17-39 as changes in the cellular constituents of the peripheral blood and bone marrow. Thus, the terms encompass medical conditions that are very diverse, if not medical opposites, from anemia (low red blood cells) to erythroleukemia (cancerous overproduction of red blood cells). Thus, a determination of enablement of claims 15 and 18 require consideration of PRV-1's effects on virtually any disease of the haematopoietic system.

Regarding the activities of PRV-1 polypeptide, the specification that PRV-1 can transduce mitogenic signals, and that overexpression of PRV-1 on granulocytes contributes to hyperproliferation of granulocytes (p. 5, lines 26-32). However, the specification contains no working examples to substantiate this assertion, and the art does not support this conclusion. See Pahl (2000, Eur. J. Biochem. 267:3395-3401), as discussed above.

Furthermore, the specification asserts that the PRV-1 polypeptide can be used to develop drugs effective for treating polycythaemia vera, based on the specification's assertion that an overproduction of PRV-1 protein is correlated with a diagnosis of polycythaemia vera (p. 7). However, this use is not enabled by the specification. As discussed above, there are no working examples correlating overexpression of PRV-1 polypeptide with any specific disease state.

Importantly, the literature clearly shows that, whereas PRV-1 **mRNA** is overexpressed in polycythaemia vera patients, there is no significant difference in PRV-1 **polypeptide** expression levels between polycythaemia vera patients and healthy control subjects. See Klippel et al., 2002, Blood 100 :2441-2448 ; especially Abstract at p. 2441 and "PRV-1 protein expression is not consistently altered in patients with polycythaemia vera" (pp. 2445-2446). Thus the art is directly contradictory to this asserted use.

The specification also discloses that PRV-1 of SEQ ID NO: 2 has growth factor activity for erythroid cells. In other words, PRV-1 can stimulate haematopoietic precursors to form erythroid cells (red blood cells). There are working examples to substantiate this assertion (see pp. 10-11 and Examples 2 and 3). Therefore, one skilled in the art would know how to use the PRV-1 polypeptide of SEQ ID NO: 2 as a drug to treat diseases characterized by a low number of red blood cells, such as anemia.

However, as explained above, the claims are much broader in scope than this. Regarding the scope of the treatable diseases encompassed by the claims, it is clear that the specification only supports treatment of diseases characterized by low red blood cell counts (such as anemia), as discussed above. Due to the large quantity of experimentation necessary to determine what other diseases can be treated with PRV-1 polypeptide, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of the effects of any protein on any specific disease in the absence of empirical data, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, regarding the scope of the structure of the PRV-1 polypeptide recited in the claims, the specification only shows that the full length PRV-1 polypeptide of SEQ ID NO: 2 has the erythroid-promoting activity. There is no guidance regarding what modifications (including deletions) that can be made to this sequence and still retain the activity required to make the polypeptide a useful drug. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid alterations are generally possible in any given protein the positions within the protein's sequence where such amino acid alterations can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may

not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claims 13, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention wherein the recited polynucleotide comprises SEQ ID NO: 1 and the recited disease is polycythaemia vera, does not reasonably provide enablement for the invention where the polynucleotide comprises fragments of SEQ ID NO: 1 or wherein the recited diseases encompass any disturbance of the haematopoietic system. The specification does not enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a process for detecting polycythaemia vera comprising detecting a polynucleotide of SEQ ID NO: 1 or a specific fragment thereof (cl. 13); or kits for detecting disturbances of the haematopoietic system such as polycythaemia vera comprising the polynucleotide of SEQ ID NO: 1, specific fragments thereof, or a structurally undefined fragment thereof (cl. 21, 22).

The specification asserts that PRV-1 is overexpressed in patients suffering from polycythaemia vera. The literature supports that PRV-1 mRNA is overexpressed in polycythaemia vera patients (see Pahl, *supra*, Klippel et al., *supra*, and Temerinac et al., 2000, Blood 95:2569-2576. However, in each case, the full coding sequence of PRV-1 was detected. Neither the specification nor the literature provides any support for the detection or use of PRV-1 DNA fragments to diagnose polycythaemia vera. Therefore, due to the large quantity of experimentation necessary to determine which fragments of SEQ ID NO; 1 can be used as a target or a probe in the detection of polycythaemia vera, the lack of direction/guidance presented in the specification regarding which structural features are required in order to retain specificity, the absence of working examples directed to use of fragments, the complex nature of the invention, the state of the prior art as reviewed above, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Regarding the scope of haematopoietic disturbances as recited in claim 22, neither the specification nor the art provide support for the concept that PRV-1 nucleic acids can be used diagnostically to detect any haematopoietic disturbance other than polycythaemia vera. In fact,

Temerinac et al. (2000, Blood 95:2569-2576) tested whether PRV-1 nucleic acids displayed altered expression levels in the haematopoietic diseases chronic myelogenous leukemia, acute myelogenous leukemia, thrombocythemia or secondary erythrocytosis. Therefore, due to the large quantity of experimentation necessary to determine what specific diseases other than polycythaemia vera are associate with an altered level or form of PRV-1 nucleic acid, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to diseases other than polycythaemia vera, the complex nature of the invention, the state of the prior art as reviewed above, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

11. Claims 1, 13, 15, 18, 21-22, 24, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to fragments of the isolated polypeptide of SEQ ID NO: 2, wherein the fragment contains at least 50 amino acids. The claims also recite a process for detecting polycythaemia vera characterized in that the PRV-1 polynucleotide is detected. The claims also recite drugs and kits comprising the polypeptides and fragments thereof. The claims recite kits comprising the claimed polynucleotide and fragments thereof.

The specification of the instant application teaches that the invention encompasses fragments of the PRV-1 polypeptide which are N-glycosylated (pg 4, lines 20-22). The

specification also discloses that "the fragments are at least 50 amino acids in length, preferably at least 100 amino acids and most preferably at least 150 amino acids" (pg 4, lines 22-25). The specification teaches that a fragment of PRV-1 polynucleotide possesses more than 100 nucleotides, preferably however, more than 300 nucleotides (pg 3, lines 21-29). The claims do not require that the nucleic acid or polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids and proteins.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of polynucleotides and polypeptides. Additionally, the description of one polynucleotide species (SEQ ID NO: 1) is not adequate written description of an entire genus of functionally equivalent polynucleotides which incorporate all variants and fragments of the nucleic acid comprising the sequence of SEQ ID NO: 1 (see claims 21 and 22, for example). The description of one polynucleotide species (SEQ ID NO: 1) is also not adequate written description of an entire genus of methods of using all possible PRV-1 polynucleotides (see claim 13, for example). Furthermore, the description of one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of

functionally equivalent polypeptides which incorporate all variants and fragments containing at least 50 amino acids of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed PRV-1 polynucleotides and polypeptides or the PRV-1 polynucleotides of the encompassed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method or method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid and amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid consisting of the sequence of SEQ ID NO: 1 and specific nucleic acids that encode full-length and mature (with and without signal peptide) PRV-1 protein; a method of detecting a specific PRV-1 nucleic acid sequence as described above; and

an isolated polypeptide consisting of the amino acid sequence of SEQ ID NO: 2 and specific amino acid ranges of SEQ ID NO: 2 directed to the full-length and mature (with and without signal peptide) PRV-1 protein, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Double Patenting

Statutory

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

12. Claim 4 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 4 of prior U.S. Patent No. 6,686,153. This is a double patenting rejection.

Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 13, 21, 22, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 18-21 of U.S. Patent No. 6,686,153. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to an isolated PRV-1 polypeptide, an isolated PRV-1 polynucleotide, and a method of detecting polycythaemia vera by detecting PRV-1 polynucleotide. **(I)** The only difference between polypeptide claims 1-3 of the '153 patent and claims 1 and 27 of the instant application is that claim 1 of the '153 patent recites full-length and mature (with and without signal peptide) PRV-1 amino acid sequences and "a antigenic fragment" of PRV-1 while claim 1 of the pending application recites full-length and mature (with and without signal peptide) PRV-1 amino acid sequences and "a fragment" PRV-1. Claim 27 of the pending application simply recites a kit comprising full-length and mature PRV-1 polypeptide, and fragments thereof. It is also noted that SEQ ID NO: 2 in both applications is identical and consists of 437 amino acids. **(II)** Claim 4 of the '153 patent recites the PRV-1 polynucleotide of SEQ ID NO: 1, including protein-encoding nucleotides, while claims 21 and 22 of the instant application recite kits comprising the PRV-1 polynucleotide of SEQ ID NO: 1, including the protein-encoding nucleotides and fragments thereof. **(III)** Finally, patented

species claims 18-21, which recite a method of diagnosing polycythaemia vera comprising detecting expression of a polynucleotide coding for human PRV-1 in a blood sample comprising granulocytes (by RT-PCR or blotting) render obvious pending genus claim 13 of a process for detecting polycythaemia vera characterized in that any PRV-1 polynucleotide (in any sample) is detected by RT-PCR or a blotting method. Therefore, the instant claims are not patentably distinct over the issued claims in U.S. patent 6,686,153.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1, 4, 13, 15, 18, 21-22, 24, and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Temerinac et al. (Leukemia Res 23(Suppl 1): S18, April 1999; "Temerinac 1999") as evidenced by Temerinac et al. (Blood 95(8): 2569-576, 2000; "Temerinac 2000").

Temerinac 1999 teaches the utilization of suppressive subtractive hybridization to isolate a novel gene termed PRV-1. The gene is highly expressed in granulocytes from polycythemia vera patients, but not detectable in normal control granulocytes. Temerinac 1999 discloses that the PRV-1 gene may be detected by Northern blot analysis. Temerinac 1999 also teaches that the PRV-1 cDNA encodes an open reading frame of 437 amino acids, which contains a signal peptide at the N-terminus and a transmembrane domain between amino acids 415 and 435. Temerinac 1999 discloses that PRV-1 contains two cysteine-rich domains homologous to those found in uPAR/Ly6 receptor superfamily. Although Temerinac 1999 does not disclose the specific nucleic acid and amino acid sequences of PRV-1, Temerinac 2000 discloses the PRV-1

nucleic acid and amino acid sequences (and their characteristics) via the same methodology as taught by Temerinac 1999 (Temerinac 2000, pg 2570-2573). Thus, Temerinac 2000 demonstrate that the missing descriptive matter is necessarily present in the Temerinac 1999 reference.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Sheppard et al. (US 6,084,088 ; issued 7/4/00 ; filed 5/6/98) is the closest prior art. Sheppard et al. disclose a polypeptide (and the nucleic acid encoding same) that is 99.2% identical to the instant SEQ ID NO: 2. However, there are two mismatches between SEQ ID NO: 2 and the polypeptide of Sheppard et al., occurring at positions 31 and 431. All of the fragments recited in claims 1 and 4 encompass at least one of these mismatched sites, and the reference does not suggest making the specific substitutions necessary to make their sequence 100% identical to the claimed sequence. Thus the reference does not read on the claimed invention. Regarding claims 21 and 22, which recite undefined fragments, the Sheppard et al. reference do not suggest that their polynucleotide Is diagnostic of any haematopoietic disorder. Therefore, the reference does not read on claims 21 or 22.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
18 July 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER